REMARKS

Reconsideration of the application in view of the amendments to the claims and the remarks presented herein.

The claims in the application are claims 18 to 33, all other claims being cancelled. The composition claims have been cancelled and all claims are now directed to methods of treatment.

Claims 1, 3, 5 to 8, 11, 12, 14, 15 and 18 have been rejected under 35 USC 103 as being obvious over Saunal et al and Maillo et al taken in view of Winters et al. The Examiner states that Saunal et al teaches a transdermal topical formulation including a solvent, absorption promoting agent, Nomegestrol as active agent and a film forming agent. Maillo et al is cited as teaching a gel-formula for topical use of progesterone compounds including Nomegestrol, ethyl alcohol, polyethylene glycol and water. The Examiner cites Winters et al as showing topical formulations of 19-nor-progesterone for systemic delivery.

Claims 9, 10, 13, 16 and 17 have been rejected under 35 USC 103 as being obvious over the same prior art taken in further view of the Merck Index, the Eibl et al patent and Remington's Pharmaceutical Sciences reference. The tertiary references are cited to show specific agents. The Examiner refutes hind sight and indicates that there is

no evidence that the evidence that Applicants have not used conventional ingredients for topical and transdermal ingredients.

Applicants respectfully traverse these grounds of rejection since the combination of the prior art made by the Examiner with the benefit of Applicants'teaching does not render the claimed methods obvious. There are basic differences between Applicants'invention and Saunal reference. The latter relates to a fluid gel which may be sprayed on the skin and namely on whatever zone of the body, on a predetermined cutaneous area. This spraying may be performed by direct spraying of the gel by means of a dosing pump with or without any propelling gais.

This sprayable gel is made with a volatile solvent having a boiling point lower than 100°C so the solvent may evaporate quickly at contact with the skin. So that this gel may be sprayed, the solvent has to be selected in such a manner as it dissolves the release matrix, the absorption promoter and the active ingredient. For this purpose, the solvent must be able to provide a homogeneous solution which may be sprayed. Accordingly, the gel is a fluid solution of low viscosity to give after spraying a covering area of 10 to 40 cm^2. This spraying after evaporation of the solvent forms a supple and resistant plastic film, not a gel. As indicated in the present application, the film forming gel is stronger, more adhesive and insures the release of the active ingredient.

The Maillos et al reference relates to 19-nor pregnane derivatives which are potent progestogens devoid of residual androgenic activity. The reference teaches oral

administration but also parental administration, intramuscular subcutaneous and percutaneous and vaginal, ocular or nasal roots in the form of solid, semi-solid or liquid dosage form and refers to all pharmaceutical compositions generally but does not teach Applicants' compositions.

The Winters reference relates to a delivery system of drugs made of a fluid solution which is sprayed using an airless pump. It results in a thin film. This film forming solution needs to be delivered using an airless pump. This implies that the film formed allows vapour penetration and would be considered breathable due to the significant volatility of the solvent, namely based on ethanol or isopropanol. This has nothing in common with the ternary or quaternary mixtures of solvent used in the present patent application where the mixtures water-ethanol – propylene glycol are not volatile and could be efficiently spread.

Synthetic progesterones have the main drawback of having very poor diffusion properties through the skin due to their lipophilic character and Applicants' invention provides a precise balance between the solubility of the active ingredient and the vehicle and its ability to diffuse through the skin towards the bloodstream. This is why the mixture proportion of the preferred solubilizing agent suitable for Applicants' invetnion is the main point of distinction with respect to the prior art. The effectiveness of the composition is the result of the proper combination and term of dosage of all the excipients.

In Applicants' invention, the preferred solubilizing agent is a ternary mixture or a quaternary mixture of 95% ethanol/water/propyleneglycol and optionally Labrasol wherein the percentage of 95% ethanol varies from 30 to 50% and the amount of water is 30 to 60% and the propyleneglycol is 2 to 20% and the Labrasol is 3 to 7%, all percentages being by weight. This composition permits nomegesterol to pass through the cutaneous barrier to obtain good clinical results when the excipient mixture proportions are properly balanced as can be seen from the examples in the application as filed.

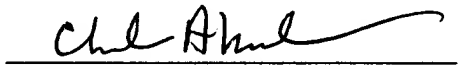
The Saunal et al compositions do not contain propylene glycol which contributes to the effectiveness of the diffusion through the skin and Saunal et al did not show any examples of compositions containing 19-nor progesterone derivatives and specifically not nomegesterol acetate. The reference taught estradiol compositions as being easily obtained and satisfactorily efficient due to the high lipophilicity of estradiol. Saunal et al only postulates the possibility that these compositions could contain nomegesterol acetate and does not teach Applicants' advantages of the compositions. There is no way to obtain Applicants' gel having systemic activity with the active ingredients being highly lipophlic. Therefore, withdrawal of these grounds of rejection is requested.

In other words, one cannot compare a liquid sprayable solution, allowing the dispensing of a drug on a large area of the skin and a gel or a film-forming gel which can only be applied on a limited area of the skin. This kind of gel is a solid gel and has to be applied on the skin, namely on the breast or the abdominal skin. It has not to become dry and it is better it remains somewhat soft and supple.

For these many reasons, Applicants think at first appropriate to discuss the two references cited by the Examiner and secondly to shift the claims to claims directed to methods of treatment using a safe and efficient amount of gel or film forming gel. Based on the experimental part Applicants think it is the way to overcome the various grounds of rejection sustained by the Examiner.

In view of the amendments to the claims and the above remarks, it is believed that the claims point out Applicants' patentable contribution. Therefore, favorable reconsideration of the application is requested.

Respectfully submitted,
Hedman and Costigan



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Enclosures